

~~40696902~~  
40268912

## DATA EVALUATION RECORD

1. Chemical: Difethialone
2. Test Material: Technical (% a.i. not specified) *Amended to 99.51% Ruzh 2-13-89.*
3. Study Type: 30-Day Dietary LC50 *See attachment under*  
*reproducibility Section*
4. Test Species: Mallard Ducks
5. Study ID: *?*  
Title: 30-day Dietary LC50 Study with LM-2219  
Technical in Mallard Ducklings.  
Author: Dale W. Fletcher  
Date: July 17, 1986  
Laboratory: Bio-Life Associates, Inc.  
*MRID 40696902*
6. Reviewed By:  
Richard Felthousen  
EFED  
Signature: *Richard Felthousen*  
Date: *10.28.88*
7. Approved By:  
Norm Cook,  
Head Section 2  
EFED  
Signature: *Norman J. Cook*  
Date: *11.1.88*
8. Conclusions:  
The study was scientifically sound and conducted in accordance with good laboratory practices, however, because the percent a.i. of the test material was not specifically mentioned the study cannot be classified as Core. The 30-day dietary LC50 is reported to be 1.9 (0.74-5.10) ppm which is considered to be very highly toxic to avian species.
9. Recommendations:  
The percent active ingredient of the test material needs to be specified in order to satisfy the data requirement.
10. Background:  
The study was submitted to satisfy Section 3 Registration Data Requirements.
11. Materials and Methods:  
A. Test Animals:  
species: Mallard ducks  
age: 5-10 days  
source: Whistling Wings  
condition: good



B. Conditions:

Temperature: 75-83 F

Photoperiod: 24 L

Housing: Wire mesh cages

Acclimation: Birds were acclimated for a sufficient period of time prior to testing.

C. Diet:

Preparation: Diet did not contain Vitamin K which could counteract effects of anticoagulant. (See Attached Sheet).

D. Treatments:

Concentrations(ppm): 256,128,64,32,16,8,4,2,1,0.5

Birds/Concentration: 10

Controls: 4 (10 birds/control)

E. Statistics:

Litchfield, J. T., Jr. and Wilcoxon, F. " A Simplified Method of Evaluating Dose-Effect Experiments, " J. Pharm & Exp. Ther. 96, 99 (1049).

F. Reported Results:

Calculated LC50:

The dietary median lethal concentration (LC50) of the test material was 1.96 ppm with 95% confidence limits of 0.74 to 5.10 ppm.

Observed Effects: Observations were made daily to ascertain the presence or absence of clinical signs indicative of the test material.

Clinical signs included lethargy, weakness, green feces and reduced food consumption. See attached sheets for complete list of observations.

Pathology: Gross pathological symptoms occurred at all levels.

Mortality: Mortality occurred up to 21 days after initial exposure.

Food Consumption: Statistically significant differences in food consumption occurred at treatment.

Body Weight: No statistically significant differences.

Statistical Analysis: See attached sheet

12. Reviewers Discussion and Interpretation of the Study:

A. Test Procedures: A 30-day rather than typical 8-day dietary study is required because of the potential for

delayed toxicity and effects associated with anticoagulant pesticides. The study was conducted in accordance with those Standard Evaluation Procedures as described in USEPA Guidance Document for conducting an avian dietary LC50 study. The reviewer believes that the results are indicative of the dietary toxicity of the material to mallard ducks.

B. Statistical Analysis: No additional work on the statistical analysis is necessary. The EEB agrees with the method used and the reported results.

C. Discussion/Results: The EEB has determined (binomial test) that an approximate LC50 for the data set is 1.4 ppm. Results calculated using the Moving Average Method show the LC50 to be 2.33 ppm. The EEB believes that the reported value, although somewhat different than the EEB's analysis is representative of the toxicity of the chemical. The chemical is considered to be very highly toxic to avian species. However, the percent active ingredient tested must be reported before the study can be used to satisfy registration requirements.

13. Adequacy of Study:

1. Category: Supplemental

*upgrade to C.*

2. Rationale: The report failed to mention the percent active ingredient of the technical grade material.

The study was scientifically sound, and conducted in accordance with the testing guidelines. Deviations from acceptable protocols were not sufficient enough to affect the results of the study.

3. Repairability: The study can be upgraded to Core if the percent active ingredient of the technical grade material is submitted for review.

*On 1-13-89 The Registrant in response to EEB's review submitted information on the percent active ingredient used in the avian dietary LC50 study (99.51%). The study now ~~satisfies~~ can be upgraded to CORE and satisfies basic data requirement for registration.*

*RWD  
2-13-89*

NOTE: BECAUSE THERE WAS CONTROL MORTALITY, AND NONE  
OF THE LOWER CONCENTRATIONS PRODUCED ZERO MORTALITY,  
THE DATA HAS BEEN SUBJECTED TO ABBOTT'S CORRECTION.

Felthousen Difethialone mallard 10-25-88

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CONC.	NUMBER EXPOSED	NUMBER DEAD	PERCENT DEAD	BINOMIAL PROB. (PERCENT)
256	9.25	9.25	100	.1953125
128	9.25	7.25	78.3784	8.984375
64	9.25	8.25	89.1892	1.953125
32	9.25	6.25	67.5676	25.39063
16	9.25	7.25	78.3784	8.984375
8	9.25	6.25	67.5676	25.39063
4	9.25	6.25	67.5676	25.39063
2	9.25	6.25	67.5676	25.39063
1	9.25	3.25	35.1351	25.39063
.5	9.25	.25	2.7027	.1953125

THE BINOMIAL TEST SHOWS THAT .5 AND 256 CAN BE  
USED AS STATISTICALLY SOUND CONSERVATIVE 95 PERCENT  
CONFIDENCE LIMITS, BECAUSE THE ACTUAL CONFIDENCE LEVEL  
ASSOCIATED WITH THESE LIMITS IS GREATER THAN 95 PERCENT.

AN APPROXIMATE LC50 FOR THIS SET OF DATA IS 1.372698

RESULTS CALCULATED USING THE MOVING AVERAGE METHOD

SPAN	G	LC50	95 PERCENT CONFIDENCE LIMITS	
5	.3082469	2.334794	1.052895	4.363936

RESULTS CALCULATED USING THE PROBIT METHOD

ITERATIONS	G	H	GOODNESS OF FIT PROBABILITY
4	.1961626	1	.347615

SLOPE = .824284  
95 PERCENT CONFIDENCE LIMITS = .4592066 AND 1.189362

LC50 = 2.898533  
95 PERCENT CONFIDENCE LIMITS = .8297246 AND 6.481888

LC10 = .083454  
95 PERCENT CONFIDENCE LIMITS = 2.052457E-03 AND .3845227

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B. Gross Pathology

Gross pathological examinations of all birds found dead during the study revealed the following:

Group	Time of Death	Date of Death	Findings
C-I	11:45 a.m.	4/28/86	Small bird; impacted rectum
C-I	1:30 p.m.	5/01/86	No abnormal tissue alterations (accidental death)
C-IV	7:35 a.m.	5/02/86	Small bird; large yolk sac in rectal area
T-I	7:55 a.m.	4/30/86	Impacted rectum with a very slight amount of blood near this area
T-II	8:00 a.m.	4/27/86	Severe subcutaneous and intramuscular diffuse red discoloration of both legs
T-II	7:35 a.m.	4/28/86	Diffuse red discoloration under the skin covering the abdomen; mild subcutaneous diffuse red discoloration of the right leg; severe subcutaneous and intramuscular diffuse red discoloration of the left leg
T-II	7:45 a.m.	5/05/86	Blood covering the down; legs swollen at the joints and down to the feet; bloody fluid in leg joints; mild intramuscular diffuse red discoloration of both legs
T-II	7:45 a.m.	5/08/86	Enlarged gall bladder; green liver lobes next to gall bladder; severe intramuscular diffuse red discoloration of both legs, watery left eye; swollen area around left eye
T-III	7:35 a.m.	4/25/86	Excess diffuse red fluid surrounding the pericardium
T-III	7:40 a.m.	4/26/86	Mild intramuscular diffuse red discoloration of the left leg; bloody fluid in the lung cavity; clotted blood in the visceral cavity
T-III	7:35 a.m.	4/28/86	Severe subcutaneous and intramuscular diffuse red discoloration of the right leg; mild subcutaneous diffuse red discoloration of the left leg

Group	Time of Death	Date of Death	Findings
T-III	3:30 p.m.	4/28/86	Diffuse red discoloration under the skin covering the abdomen; diffuse red discoloration in the neck area; severe intramuscular diffuse red discoloration of the left leg
T-III	7:35 a.m.	4/29/86	Bloody fluid surrounding the pericardium; mild intramuscular diffuse red discoloration of the left leg
T-III	9:30 a.m.	4/30/86	Severe subcutaneous and intramuscular diffuse red discoloration of both legs
T-III	9:30 a.m.	4/30/86	Severe subcutaneous and intramuscular diffuse red discoloration of both legs; bloody fluid surrounding the pericardium
T-IV	7:40 a.m.	4/26/86	Severe intramuscular diffuse red discoloration of the right leg; bloody fluid surrounding the pericardium
T-IV	7:35 a.m.	4/28/86	Very mild subcutaneous diffuse red discoloration of the right leg
T-IV	7:35 a.m.	4/29/86	Clotted blood in the lung cavity, body cavity, and neck area; mild subcutaneous diffuse red discoloration of the right leg
T-IV	3:40 p.m.	4/30/86	Clotted blood in the visceral cavity; blood-filled intestines
T-IV	7:45 a.m.	5/01/86	Mild intramuscular diffuse red discoloration of the left leg; severe intramuscular diffuse red discoloration of the right leg; rectum impacted with semi-solid feces
T-IV	7:45 a.m.	5/01/86	Blood-filled cyst on the mandible; blood in the neck area; mild intramuscular diffuse red discoloration of the right leg; severe intramuscular diffuse red discoloration of the left leg
T-IV	7:43 a.m.	5/03/86	Mild intramuscular diffuse red discoloration of both legs; large yolk sac; blood in the neck area
T-V	7:40 a.m.	4/26/86	Small bird; mild intramuscular diffuse red discoloration of the left leg

Group	Time of Death	Date of Death	Findings
T-V	9:00 a.m.	4/26/86	Bloody fluid surrounding the pericardium; severe intramuscular diffuse red discoloration of the left leg; mild intramuscular diffuse red discoloration of the right leg
T-V	8:00 a.m.	4/27/86	Severe subcutaneous and intramuscular diffuse red discoloration of the left leg; bloody fluid surrounding the pericardium
T-V	7:35 a.m.	5/02/86	Severe subcutaneous and intramuscular diffuse red discoloration of the left leg; clotted blood in the abdominal cavity
T-V	7:40 a.m.	5/04/86	Severe subcutaneous and intramuscular diffuse red discoloration starting at the left leg, under the skin, up along the side of the body, and including the neck area
T-V	7:45 a.m.	5/05/86	Mild intramuscular diffuse red discoloration of the right leg; severe intramuscular diffuse red discoloration of the left leg; blood surrounding the pericardium; air-filled intestines which are yellow in color
T-V	2:30 p.m.	5/06/86	Severe intramuscular diffuse red discoloration of the left leg; mild intramuscular diffuse red discoloration of the right leg; blood in the lung cavity
T-VI	11:00 a.m.	4/24/86	Mild intramuscular diffuse red discoloration of both legs; clotted blood by the heart; blood in the neck region
T-VI	7:35 a.m.	4/25/86	Diffuse red discoloration under the skin on the body cavity; excess diffuse red fluid surrounding the pericardium
T-VI	7:40 a.m.	4/26/86	Severe intramuscular diffuse red discoloration of the left leg; mild intramuscular diffuse red discoloration of the right leg
T-VI	7:35 a.m.	4/28/86	Mild subcutaneous diffuse red discoloration of the right leg
T-VI	7:55 a.m.	4/30/86	Severe intramuscular diffuse red discoloration of the left leg; mild intramuscular diffuse red discoloration of the right leg

Group	Time of Death	Date of Death	Findings
T-VI	7:55 a.m.	4/30/86	Mild intramuscular diffuse red discoloration of both legs; clotted blood in the visceral cavity; diffuse red discoloration under the skin of the abdomen
T-VI	7:35 a.m.	5/02/86	Severe subcutaneous and intramuscular diffuse red discoloration of the left leg; extremely large amount of clotted blood in the neck area
T-VI	7:45 a.m.	5/09/86	Cloudy white opacity present on the surface of the pupil area of the right eye; severe intramuscular diffuse red discoloration of the right leg; mild intramuscular diffuse red discoloration of the left leg; enlarged cloaca at the rectal area which is filled with a cloudy light green liquid
T-VII	7:45 a.m.	4/23/86	No abnormal tissue alterations
T-VII	3:00 p.m.	4/25/86	Mild intramuscular diffuse red discoloration of both legs
T-VII	7:40 a.m.	4/26/86	Severe subcutaneous and intramuscular diffuse red discoloration of the right leg; bloody fluid in the lung cavity
T-VII	7:35 a.m.	4/28/86	Mild subcutaneous diffuse red discoloration of the left leg
T-VII	7:35 a.m.	4/29/86	Bloody fluid surrounding the pericardium; severe subcutaneous and intramuscular diffuse red discoloration of the left leg
T-VII	2:45 p.m.	4/29/86	Severe subcutaneous and intramuscular diffuse red discoloration of both legs; body cavity blood-filled; severely bloody neck area
T-VII	7:45 a.m.	5/05/86	Mild intramuscular diffuse red discoloration of both legs
T-VIII	2:10 p.m.	4/23/86	Slight intramuscular diffuse red discoloration of both legs; slight diffuse red discoloration of the intestinal vessels
T-VIII	8:00 a.m.	4/24/86	Very slight subcutaneous diffuse red discoloration of both legs; large blood filled cyst on the mandible



Group	Time of Death	Date of Death	Findings
T-VIII	7:35 a.m.	4/25/86	Severe subcutaneous and intramuscular diffuse red discoloration of the right leg
T-VIII	8:00 a.m.	4/27/86	Diffuse red discoloration under the skin covering the abdomen; very pale liver
T-VIII	7:35 a.m.	4/28/86	Mild subcutaneous diffuse red discoloration of both legs
T-VIII	7:35 a.m.	4/28/86	Severe subcutaneous and intramuscular diffuse red discoloration of the right leg
T-VIII	3:30 p.m.	4/28/86	Very slight intramuscular diffuse red discoloration of both legs; rectum impacted with food and water
T-VIII	7:43 a.m.	5/03/86	Severe subcutaneous and intramuscular diffuse red discoloration of the right leg; mild subcutaneous diffuse red discoloration of the left leg; bloody fluid surrounding the pericardium
T-VIII	7:35 a.m.	5/06/86	Cloudy white opacity present on the surface of the pupil areas of both eyes; mild intramuscular diffuse red discoloration of both legs; large amount of clotted blood in the lung and abdominal cavities
T-IX	8:00 a.m.	4/27/86	Blood around the edges of the mouth; severe subcutaneous and intramuscular diffuse red discoloration of the left leg; mild subcutaneous diffuse red discoloration of the right leg
T-IX	8:00 a.m.	4/27/86	Very pale liver; mild intramuscular diffuse red discoloration of the right leg
T-IX	11:45 a.m.	4/28/86	Mild intramuscular diffuse red discoloration of the left leg; severe intramuscular diffuse red discoloration of the right leg
T-IX	7:35 a.m.	5/06/86	Green feces on the down; cloudy white opacity on the surface of the pupil areas of both eyes; mild intramuscular diffuse red discoloration of the left leg; diffuse red discoloration under the skin, along the left side of the body and including the neck area; clotted blood in the lung and abdominal cavities

Group	Time of Death	Date of Death	Findings
T-IX	7:35 a.m.	5/07/86	Rectum impacted with semi-solid feces; enlarged cloaca which is filled with semi-solid feces; severe subcutaneous and intramuscular diffuse red discoloration of the right leg; mild subcutaneous diffuse red discoloration of the left leg
T-IX	1:00 p.m.	5/07/86	Severe intramuscular diffuse red discoloration of both legs; clotted blood in the abdominal cavity
T-IX	7:45 a.m.	5/08/86	Mild intramuscular diffuse red discoloration of both legs; green liver lobes next to the gall bladder
T-IX	3:00 p.m.	5/08/86	Mild subcutaneous diffuse red discoloration of both legs; enlarged proventriculus which is impacted with food
T-X	8:00 a.m.	4/24/86	Severe intramuscular diffuse red discoloration of the left leg; mild intramuscular diffuse red discoloration of the right leg
T-X	9:30 a.m.	4/25/86	Severe intramuscular diffuse red discoloration of both legs
T-X	8:00 a.m.	4/27/86	Very severe subcutaneous and intramuscular diffuse red discoloration of the right leg
T-X	7:35 a.m.	4/28/86	Severe subcutaneous and intramuscular diffuse red discoloration of the right leg
T-X	7:35 a.m.	4/28/86	Severe subcutaneous and intramuscularly diffuse red discoloration of the right leg
T-X	7:35 a.m.	4/29/86	Bloody fluid surrounding the pericardium; severe intramuscular diffuse red discoloration of the right leg
T-X	7:45 a.m.	5/01/86	Severe subcutaneous and intramuscular diffuse red discoloration of the right leg; bloody fluid surrounding the pericardium
T-X	7:40 a.m.	5/04/86	Severe subcutaneous and intramuscular diffuse red discoloration of both legs and also under the skin covering the abdomen and rib cage area

Group	Time of Death	Date of Death	Findings
T-X	8:15 a.m.	5/11/86	Severe subcutaneous and intramuscular diffuse red discoloration of the left leg; mild subcutaneous diffuse red discoloration of the right leg
T-X	7:35 a.m.	5/12/86	Severe intramuscular diffuse red discoloration of the right leg; mild intramuscular diffuse red discoloration of the left leg; pooled blood under the skin in the right pectoral area; green liver lobes next to gall bladder; cloaca enlarged at rectal area and filled with semi-solid light green feces; blood exuding from the nostrils; area around the left eye is puffy and a bloody fluid is present

Gross pathological examinations of selected birds sacrificed at the close of the investigation revealed no abnormal tissue alterations in 26 of the 29 birds examined. One T-II bird and one T-V bird had diffuse red discoloration of the intestinal vessels. Another T-V bird had very mild intramuscular diffuse red discoloration of the left leg.

Lipha Laboratories - Research Center  
B.P. 8481 - 69359 Lyon Cedex 08

CERTIFICATE OF ANALYSIS

DUPLICATA

DUPLICATA

: NAME OF THE PRODUCT:	LM 2219	:
: ORIGIN: JJB	: ANALYSIS NUMBER: L 2816	:
: REFERENCE: JCC3891	: DATE OF ANALYSIS: 07/08/85	:
: MANUFACTURING DATE: 2/25/85	: TECHNICAL REF.: TEC/LM2219/1	:

: CONTROLS PERFORMED :	SPECIFICATIONS :	VALUES FOUND :
:ORGANOLEPTIC	:	:
:CHARACTERISTICS	: POWDER	: IN CONFORMANCE
:PHYSICOCHEMICAL	:	:
:CHARACTERISTICS	:	:
: .SOLUBILITIES	:	: IN CONFORMANCE
: .U.V. SPECTER	:	:
: maximum 1	: 215-219 nm	: 216.9 nm
: maximum 2	: 258-262 nm	: 259.8 nm
: maximum 3	: 326-330 nm	: 328.5 nm
: at 1%-cm	: CLOSE TO 780	: 772.6
: IDENTIFICATION	:	:
: .I.R. SPECTER	: IDENTICAL TO	: IN CONFORMANCE
:	: CONTROL	:
: TESTS	:	:
: .HUMIDITY LEVEL	: <=1%	: 0.0097%
: .SULPHURIC ASH	: <=0.2%	: 0.0365%
: .DIASTEREOISOMERES	:	:
: majority	: 85-100%	: 94.88%
: .SYNTHESIS IMPURITIES:	:	:
: global content	: <1.2%	: 0.569%
: DOSAGE	: 98-102%	: 99.51%

: DATE: 07/30/86	: CONCLUSION: IN CONFORMANCE	:
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Signed: B. LABARTHE